REMARKS/ARGUMENTS

Claims 1-21 are pending in the instant application. The following remarks are believed to be fully responsive to the Office Action.

35 USC § 102(b) Rejection

Claims 1, 3-4, 7-9, 11-12, 14-15, 17, and 19-20 stand rejected under 35 USC § 102(b) as being anticipated by U.S. Patent No. 5,948,940 to Malthe-Sorenssen et al. ("Malthe-Sorenssen").

Malthe-Sorenssen discloses the use of 2-methoxy-ethanol. On pages 3 and 4 of the Office Action dated October 29, 2007, the Examiner holds that this solvent is a C_1-C_5-monoalkylether of a C_3-C_{10} alkylene-glycol. We respectfully submit that this is not the case since "ethanol" in 2-methoxy-ethanol only comprises two carbon atoms and three to ten carbon atoms would be necessary to fall under "C_3-C_{10} alkylene-glycol".

Accordingly, Applicants respectfully request that the Examiner withdrawal the rejections for claims 1,3-4, 7-9, 11-12, 14-15, 17, and 19-20 under 35 U.S.C. §103(a) and direct that these claims be allowed.

35 USC § 103 (a) Rejection

Claims 1-2, 5-6, 10, 13, 16, 18, and 21 stand rejected under 35 USC § 103(a) as being unpatentable over U.S. Patent No. 5,948,940 to Malthe-Sorenssen et al. ("Malthe-Sorenssen").

On page 5 of the Office Action, the Examiner holds that Malthe-Sorenssen describes using 2-methoxy-ethanol as solvent in the production of iohexol. The Examiner further holds that Malthe-Sorenssen clearly suggests to one having ordinary skill in the art the use of similar solvents, that it is routine for a skilled artisan to use art recognizing alternative solvents, and that it would have been obvious to a person skilled in the art to use 1-methoxy-2-propanol in Malthe-Sorenssen. Applicants respectfully disagree. Malthe-Sorenssen describes a process for the production of iohexol where the solvent used is 2-methoxy-ethanol. Malthe-Sorenssen does not teach, describe, or suggest using similar solvents or any other solvents other than 2-methoxy-ethanol. There are no indications in Marlthe-Sorenssen regarding the use of alternative solvents, there are no indications regarding which solvent might be used as an alternative solvent and there are no indications that alternative solvents would give better results. Malthe-Sorenssen clearly suggests the use of 2-methoxy-ethanol and no other alternatives. Applicants respectfully wish to remind the Examiner that it is impermissible within the framework of 35 U.S.C. §103 to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one skilled in the

art. *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443 (Fed. Cir. 1986). (emphasis added). Applicants further note that "the prior art itself must provide a motivation or reason for the worker in the art, without the benefit of the Applicant's specification, to make necessary changes in the reference device". See, *Ex parte Chicago Rawhide Manufacturing Co.*, 226 U.S.P.Q. 438 (PTO Bd. App. 1984).

Disregarding the fact that Malthe-Sorenssen does not teach, disclose, or suggest the use of alternative solvents, one skilled in the art would in fact not have a reasonable expectation of success when using 1-methoxy-2-propanol. The fact that a solvent is known for its use as the dominant solvent in the crystallisation step of the same process would clearly teach away from using the same in the alkylation step. 'Teaching away' simply means teaching a solution that would not lead to the claimed subject matter. As noted by the Federal Circuit:

A reference may be said to teach away when a person of ordinary skill, upon [examining]

> the reference would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. (emphasis added).

Para-Ordnance Mfg. v. SGS Importers Int'l, 73 F.3d 1085 (Fed. Cir. 1995).

In the alkylation step of Malthe-Sorenssen it is required that the solvent shows good solubility for 5-(acetamido)-N,N'bis(2,3-dihydroxypropyl)-2,4,6-triiodoisophtalamide and that the product (iohexol) does not precipitate during the reaction, whereas in the purification step the solvent used should show little solubility for the product (iohexol). A person skilled

in the art would therefore not expect that 1-methoxy-2-propanol could be used as the dominant solvent in both the alkylation and the purification step, and would not think or suggest using 1-methoxy-2-propanol as an alternative to 2-methoxy-ethanol in the production described by Malthe-Sorenssen. Malthe-Sorenssen describes using 2-methoxy-ethanol as a solvent in the purification step, however, 2-methoxy-ethanol is not the dominant solvent in the solvent mixture used in this step. The solvent mixture only comprises a small amount of 2-methoxy-ethanol, see claim 1 of Malthe-Sorenssen.

Furthermore, examples 1-3 in the present invention show that although not expected, the use of 1-methoxy-2-propanol results in a higher content of Iohexol and less impurities in the product compared to Examples 1-2 in Malthe-Sorenssen. Table 1 compares the results of using the two solvents in the alkylation step, and Table 2 compares the results after both alkylation and crystallisation.

Table 1

	2-methoxy-ethanol % (Malthe-Sorenssen example 1)	1-methoxy-2-propanol % (instant application example 1)	1-methoxy-2-propanol % (instant application example 2)
Iohexol	97,9	98,1	98,3
5-acetamide	1,03	1,17	0,68
O-alkylated substances	0,56	0,58	0,81
Other impurities	0,56	0,1	0,3

Table 2

	2-methoxy-ethanol % (Malthe-Sorenssen example 2)	1-methoxy-2-propanol % (instant application example 3)
Iohexol	99,1	99,3

5-acetamide	0,28	0,15
O-alkylated substances	0,51	0,45
Other impurities	0,15	0,11

To expect one skilled in the art reading Malthe-Sorenssen to use alternative solvents, and to define 1-methoxy-2-propanol as a similar solvent to 2-methoxy-ethanol and then further hold that it would be obvious to use 1-methoxy-2-propanol instead of 2-methoxy-ethanol with a reasonable expectation of success would clearly involve using hindsight by now knowing that the use of this solvent actually gives higher content of Iohexol and less impurities than the use of 2-methoxy-ethanol.

Accordingly, Applicants respectfully request that the Examiner withdrawal the rejections for claims 1-2, 5-6, 10, 13, 16, 18, and 21 under 35 U.S.C. §103(a) and direct that these claims be allowed.

CONCLUSION

Upon entry of this Amendment, claims 1-21 remain pending. Applicants submit that all outstanding issues have been addressed, and that claims 1-21 are in condition for allowance, which action is earnestly solicited.

Again, the Commissioner is hereby authorized to charge any fees under 37 CFR §1.16(j) or 37 CFR 1.136(a) which may be required, or credit any overpayment, to Deposit Account No. 502-665 in the name of GE Healthcare, Inc.

Should any other matters require attention prior to allowance of the application, it is requested that the Examiner contact the undersigned.

Respectfully submitted,

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